

AMENDMENT AND RESPONSE UNDER 37 C.F.R.1.111

Serial No.: 09/574460

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Filed: May 18, 2000

Docket No.: 875.009US1

Title: PRODUCTION OF COMPLEX CARBOHYDRATES

In the Claims

Claims 1-29. (Cancelled)

- E¹
- Claim 30. (New) A process for the production of a *Haemophilus influenzae*-specific lipooligosaccharide (LOS) which comprises the steps of:
- (a) growing in a culture medium ~~gram-negative bacteria~~ comprising (i) a core lipid structure containing a terminal heptose and (ii) a DNA sequence comprising a *rfe* gene, and (iii) an isolated DNA sequence comprising a lipooligosaccharide-synthesis gene G (*lsgG*) from *Haemophilus influenzae*, wherein *lsgG* encodes LsgG, and wherein the *rfe* is regulated by LsgG such that a *H. influenzae*-specific LOS is synthesized by the addition of an acceptor molecule to the terminal heptose molecule; and
 - (b) recovering the *H. influenzae*-specific LOS from the culture medium.
- Claim 31. (New) The process of claim 30, wherein the bacteria are *Escherichia coli*.
- Claim 32. (New) The process of claim 31, wherein the bacteria are *Escherichia coli* K-12 strain JM 109.
- Claim 33. (New) The process of claim 30, wherein the bacteria are *Salmonella minnesota*.
- Claim 34. (New) The process of claim 30, wherein the acceptor molecule is N-acetylglucosamine.
- Claim 35. (New) The process of claim 30, wherein the *rfe* gene is from *Haemophilus influenzae*.
- Claim 36. (New) The process of claim 30, wherein the DNA sequence comprising a *rfe* gene is part of the gram-negative bacterial genome.

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cont.
- Claim 37. (New) The process of claim 30, wherein the isolated DNA sequence comprising the *lsgG* is contained in a vector.
- Claim 38. (New) The process of claim 30, wherein the bacteria further comprise a glycosyltransferase.
- Claim 39. (New) A process for the production of a complex carbohydrate comprising the steps of:
- (a) growing in a culture medium gram-negative bacteria comprising (i) a core lipid structure containing a terminal heptose and (ii) a DNA sequence comprising a *rfe* gene, and (iii) an isolated DNA sequence comprising a liposaccharide-synthesis gene G (*lsgG*) from *Haemophilus influenzae*, wherein *lsgG* encodes LsgG, and wherein the *rfe* is regulated by LsgG such that a complex carbohydrate is synthesized by the addition of an acceptor molecule to the heptose molecule; and
 - (b) recovering the complex carbohydrate from the culture medium.
- Claim 40. (New) The process of claim 39, wherein the bacteria are *Escherichia coli*.
- Claim 41. (New) The process of claim 40, wherein the bacteria are *Escherichia coli* K-12 strain JM 109.
- Claim 42. (New) The process of claim 39, wherein the bacteria are *Salmonella minnesota*.
- Claim 43. (New) The process of claim 39, wherein the acceptor molecule is N-acetylglucosamine.
- Claim 44. (New) The process of claim 39, wherein the *rfe* gene is from *Haemophilus influenzae*.

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CONT.
- Claim 45. (New) The process of claim 39, wherein the DNA sequence comprising a *rfe* gene is part of the gram-negative bacterial genome.
- Claim 46. (New) The process of claim 39, wherein the isolated DNA sequence comprising the *lsgG* is contained in a vector.
- Claim 47. (New) The process of claim 39, wherein the bacteria further comprise a glycosyltransferase.
- Claim 48. (New) A method of modifying a terminal heptose of a lipopolysaccharide (LPS) or lipooligosaccharide (LOS) core structure of a gram-negative bacterial species containing a *rfe* gene comprising regulating the *rfe* gene with a protein encoded by an isolated *lsgG* gene from *Haemophilus influenzae* such that an N-acetyl glucosamine is added onto the terminal heptose.
- Claim 49. (New) The method of claim 48 wherein the bacteria are *Escherichia coli*.
- Claim 50. (New) The method of claim 49, wherein the bacteria are *Escherichia coli* K-12 strain JM 109.
- Claim 51. (New) The method of claim 48, wherein the bacteria are *Salmonella minnesota*.
- Claim 52. (New) The method of claim 48, wherein the *rfe* gene is from *Haemophilus influenzae*.
- Claim 53. (New) The method of claim 48, wherein the *rfe* gene is part of the gram-negative bacterial genome.

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cont.

Claim 54. (New) The method of claim 48, wherein the isolated *lsgG* gene is contained in a vector.

Claim 55. (New) The method of claim 48, wherein the bacteria further comprise a glycosyltransferase.

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Interview Summary

Applicants' Representative thank Examiners Yong Pak and Ponnathapu Achutamurthy for courtesies extended during the personal interview conducted on April 28, 2003. During the interview, the 35 U.S.C. § 103 rejections were discussed.

Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks presented herein, is respectfully requested. Claims 1-29 are cancelled. Claims 30-55 are newly added. Claims 1-29 are cancelled and re-entered as new claims 30-55 due to discrepancies recently discovered between the "Marked-up Claim Sets" and the "Clean Version of Pending Claims" filed in previous amendments. The pending claims are claims 30-55. New claims 30-55 are fully supported by the specification as originally filed, and no new subject matter has been added.

Support for the term "LsgG" in newly added claims 30 and 38 is found, for example, in the specification at page 5, lines 2-3.

Support for the term "LsgG" in newly added claims 30 and 38 is found, for example, in the specification at page Example 6 and Figure 1.

Support for the phrase "rfe is regulated by LsgG" in newly added claims 30 and 38 is found, for example, in the specification at page 5, lines 2-3 and page 7, lines 11-12.

Support for newly added claims 37, 46 and 54 is found, for example, in the specification at page 4, lines 13-14 and 25-29; page 5, lines 3-6; page 7, lines 15-19 and 23-28; as well as in claims 8-9 as originally filed. It is submitted that due to a typographical error, the term "glycotransferase" as opposed to the term "glycosyltransferase" appears in the specification. The Examiner's attention is directed to page 6 of the Office Action mailed May 7, 2001, wherein the Examiner noted this typographical error.

The 35 U.S.C. § 103 Rejection of the Claims

The Examiner rejected claims 6-8, 11-12, 18-21 and 23-28 under 35 U.S.C. § 103(a) as being unpatentable over McLaughlin *et al.* (*Journal of Endotoxin Research*, 1, 165 (1994)) in